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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/562,086

12/23/2005

Peter J. Quesenberry

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EXAMINER

AFREMOVA, VERA

ART UNIT

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1657

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/562,086	<b>Applicant(s)</b> QUESENBERRY, PETER J.	
	<b>Examiner</b> Vera Afremova	<b>Art Unit</b> 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 14-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/17/07; 2/27/06</u>  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of the group I, claims 1-12, in the reply filed on 12/07/2007 is acknowledged. The traversal is on the ground(s) that the examination of all groups will have overlapping search and that there is no another method for making the product as claimed such as differentiated hematopoietic cells. This argument does not have persuasive grounds because this application is a 371 application. The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The corresponding special technical feature such as bone marrow-derived hematopoietic cells intended for treating cytopenia are known in the art. For example: see US 6,495,365 (col. 1, lines 40-43, 51-55 and col. 3, lines 46). Thus, unity of inventions is lacking. See MPEP 1850. 37 CFR 1.475.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 12/07/2007.

Claims 1-13 are under examination in the instant office action.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-9, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hagihara et al. (IDS reference).

Claims are directed to a method for the production of differentiated hematopoietic cells wherein the method comprises step of culturing bone marrow stem cells under conditions that promote synchronous progression through the cell cycle, step of contacting the cells with a growth factor or a cytokine at predetermined phase of the cell cycle and step of subculturing the cells until differentiated hematopoietic cells are produced. Some claims are further drawn to contacting and subculturing cells with the growth factor such as GM-CSF. Some claims are further drawn to culturing cells under conditions that promote synchronous progression through the cell cycle such as culturing in the presence of steel factor, thrombopoietin and FLT-3 ligand. Some claims are further drawn to subculturing cells for about 14 days. Some claims are further drawn to additional step of isolating the differentiated hematopoietic cells from the subculture. Some claims are further drawn to the differentiated hematopoietic cells “comprising” megakaryocytes, granulocytes and platelets.

Hagihara et al. disclose a method for the production of differentiated hematopoietic cells including dendritic cells wherein the method comprises 1) step of culturing CD34+ bone marrow stem cells in the presence of steel factor, thrombopoietin and FLT-3 ligand or under conditions that promote synchronous progression through the cell; 2) subsequent step of contacting the cells with growth factor GM-CSF at a predetermined time and 3) subculturing the cells with a growth factor GM-CSF for up to 14 days or about 14 days. (entire document including abstract and page 49 at section 2.4 “Culture system”). The method taught by Hagihara et al. comprises identical

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active steps and it results in the production of the differentiated hematopoietic cells as required by the claimed method and, thus, the cited reference by Hagihara et al. clearly anticipates claimed invention of the instant claims 1-4 and 13. Although production or generation of dendritic cells is a primary goal of the cited reference by Hagihara et al., the dendritic cells were not the sole cellular product of the disclosed culturing method and, thus, the final subculture after subculturing with maturation factors including GM-CSF and/or steel factor is reasonably expected to “comprise” at least some amounts of megakaryocytes, granulocytes and platelets within the broadest reasonable meaning of the claims 7-9 and 12.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 rejected under 35 U.S.C. 103(a) as being unpatentable over Hagihara et al. (IDS reference) taken with Feng Yan et al. (Blood, November 2000, Vol. 96, No. 11, part 1, 680a), Klabusay et al. (Blood, November 2002, Vol. 100, No. 11, Abstract No. 4118), Ramsfjell et al. (Blood, December 1996, Vol. 88, No. 12, pages 4481-4492) and Messner et al. (Blood, November 1987, Vol. 70, No. 5, pages 1425-1432).

Claims are directed to a method for the production of differentiated hematopoietic cells wherein the method comprises step of culturing bone marrow stem cells under conditions that promote synchronous progression through the cell cycle, step of contacting the cells with a growth factor or a cytokine at predetermined phase of the cell cycle and step of subculturing the

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cells until differentiated hematopoietic cells are produced. Some claims are further drawn to contacting and subculturing cells with the growth factor such as GM-CSF. Some claims are further drawn to culturing cells under conditions that promote synchronous progression through the cell cycle such as culturing in the presence of steel factor, thrombopoietin and FLT-3 ligand. Some claims are further drawn to subculturing cells for about 14 days. Some claims are further drawn to additional step of isolating the differentiated hematopoietic cells from the subculture. Some claims are further drawn to the differentiated hematopoietic cells “comprising” megakaryocytes, granulocytes and platelets. Some claims are further drawn to the predetermined phase of the cell cycle being mid-S phase or late S phase.

The reference by Hagihara et al. is relied upon as explained above for the disclosure of a method for the production of differentiated hematopoietic cells from bone marrow hematopoietic stem cells by changing the cytokine cocktail combination of steel factor (SCF), thrombopoietin (TPO) and FLT-3 ligand (FLT3) to other factors including GM-CSF.

The cited reference by Hagihara et al does not clearly recognize that the cell culturing in the presence of steel factor (SCF), thrombopoietin (TPO) and FLT-3 ligand (FLT3) promotes synchronous progression of cells through the cell cycle. But the reference by Yan et al. provides for the teaching that combination of SCF, TPO and FLT-3 stimulates hematopoietic bone marrow cells to enter into synchronous cell cycle (abstract).

The cited reference by Hagihara et al. is lacking particular disclosure about the use of G-CSF for generating differentiated hematopoietic cells. However, the reference by Klabusay et al. teaches that hematopoietic stem cells are able to regenerate hematopoiesis in all lineages and that addition of G-CSF in particular will significantly increase the number of matured cells

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including granulocytes (see abstract). The reference by Ramsfjell et al. teaches that the use of factor SCF enhances megakaryocyte differentiation and production from stem cells.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify method of Hagihara et al. by adding G-CSF and steel factor (SCF) during subsequent culturing/subculturing steps with a reasonable expectation of success in producing differentiated hematopoietic cells including megakaryocytes and granulocytes because the prior art teaches and suggests the use of G-CSF and SCF for enhancing production of granulocytes and megakaryocytes. It is well known that platelets are products of megakaryocytes. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Further, the reference by Messner et al. teaches that cell cycle studies and stem cell engraftment studies indicate that the higher than normal proportions of multipotential hematopoietic cells are present in S phase during progression of the hematopoietic cells through the cell cycles (see abstract). Thus, one of skill in the art would have been motivated to contact the hematopoietic stem cells with maturation factors at the time of cell progression through S-phase for the expected benefits in maximizing yields of matured differentiated hematopoietic cells derived from the stem cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1657

March 14, 2008

VERA AFREMOVA

PRIMARY EXAMINER

/Vera Afremova/  
Primary Examiner, Art Unit 1657